BIOLOGICAL FLUID FILTER AND SYSTEM

This application claims the benefit of U.S. provisional patent application 60/102,973, filed October 2, 1998, which is incorporated by reference.

TECHNICAL FIELD

This invention relates to a filter for processing a biological fluid, more particularly, a filter that provides a leukocyte-depleted biological fluid. Preferably, the filter provides a biological fluid that is substantially free of blood cells.

BACKGROUND OF THE INVENTION

Blood contains a number of components, including plasma, platelets, red blood cells, as well as various types of white blood cells (leukocytes). Blood components may be separated, and further processed, for a variety of uses, particularly as transfusion products. Illustratively, red blood cells (typically concentrated as packed red blood cells), plasma, and platelets (typically concentrated as platelet concentrate), can be separately administered to different patients. Some components, e.g., plasma and/or platelets, can be pooled before administration, and plasma can be further processed, e.g., fractionated to provide enriched components for a variety of uses.

Unfortunately, some material is undesirably present in transfusion product. For example, while leukocytes combat infection and engulf and digest invading microorganisms and debris, the presence of leukocytes in transfusion products can be undesirable, since, for example, they may cause adverse effects (e.g., a febrile reaction) in the patient receiving the transfusion. Additionally, platelet-containing transfusion products and plasma-rich transfusion products should be substantially free of red blood cells, since the presence of a significant level of red blood cells in the transfusion product (particularly if the transfusion products

have been pooled) can lead to an adverse immune response by the patient.

However, some commercially available filters have suffered from a number of drawbacks. For example, some filters fail to remove the desired level and/or types of material, or have an undesirably large hold up volume, or cause processing time to be increased. Alternatively, or additionally, the use of some filters requires a labor- and/or time-intensive effort.

Accordingly, there is a need in the art for a filter for use with biological fluids such as blood and blood components, particularly for the production of plasma-rich blood products, that minimizes the contamination of the plasma-rich blood product by leukocytes and red blood cells. These and other advantages of the present invention will be apparent from the description as set forth below.

SUMMARY OF THE INVENTION

In accordance with an embodiment of the invention, a filter device for providing a plasma-rich biological fluid substantially free of leukocytes comprises a filter including a first filter element and a second filter element, wherein the first filter element comprises a porous fibrous leukocyte depletion medium, and the second filter element, arranged downstream of the first filter element, comprises a porous membrane. Methods for using the filter device, and systems including the filter device are also provided.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is an embodiment of a filter device according to the present invention, including a cross-sectional view of a filter having a first filter element and a second filter element.

Figure 2 is an embodiment of a system including a filter device according to the present invention.

SPECIFIC DESCRIPTION OF THE INVENTION

In accordance with an embodiment of the present invention, a filter device for processing a biological fluid comprises a housing having an inlet and an outlet and defining a fluid flow path between the inlet and the outlet, a filter disposed in the housing across the fluid flow path, the filter comprising a first filter element comprising a porous fibrous leukocyte depletion medium having a CWST of at least about 70 dynes/cm, and a second filter element comprising a porous membrane having a pore size of about 5 micrometers or less, said second filter element being disposed downstream of the first filter element, wherein the filter is arranged to allow plasma to pass therethrough and substantially prevent the passage of leukocytes therethrough.

In another embodiment, a filter device for processing a biological fluid comprises a housing having an inlet and an outlet and defining a fluid flow path between the inlet and the outlet, a filter disposed in the housing across the fluid flow path, the filter comprising a first filter element comprising a porous fibrous red cell barrier and leukocyte depletion medium having a CWST of at least about 70 dynes/cm, and a second filter element comprising a porous membrane having a pore size of about 5 micrometers or less, said second filter element being disposed downstream of the first filter element, wherein the filter is arranged to allow plasma to pass therethrough and substantially prevent the passage of leukocytes therethrough.

In a preferred embodiment, the filter is arranged to provide a substantially cell-free plasma-containing fluid.

A method for processing a biological fluid according to an embodiment of the invention comprises passing a leukocyte-containing plasma-rich biological fluid through a filter device comprising a filter including a fibrous leukocyte depletion medium and a membrane, and collecting a filtered plasma-rich biological fluid substantially free of leukocytes.

In accordance with another embodiment of the invention, a method for processing a biological fluid comprises passing

a leukocyte-containing plasma-rich biological fluid through a filter device comprising a filter including a fibrous red blood cell barrier medium and a membrane, and collecting a filtered plasma-rich biological fluid substantially free of leukocytes.

A method for processing a biological fluid provided by another embodiment of the invention comprises processing a biological fluid to provide a supernatant layer comprising a leukocyte-containing plasma-rich fluid, and a sediment layer comprising a red blood cell-containing fluid, passing the leukocyte-containing plasma-rich fluid through a filter device comprising a filter including a fibrous leukocyte depletion medium and a membrane, and collecting a filtered plasma-rich fluid substantially free of leukocytes.

A preferred embodiment of a method according to the invention comprises processing a biological fluid to provide a substantially cell-free plasma-containing fluid.

A system according to an embodiment of the invention comprises a filter device, interposed between, and in fluid communication with, at least two containers such as plastic blood bags. In one preferred embodiment, the system comprises a closed system.

As used herein a biological fluid includes any treated or untreated fluid associated with living organisms, particularly blood, including whole blood, warm or cold blood, and stored or fresh blood; treated blood, such as blood diluted with at least one physiological solution, including but not limited to saline, nutrient, and/or anticoagulant solutions; blood components, such as platelet concentrate (PC), platelet-rich plasma (PRP), platelet-poor plasma (PPP), platelet-free plasma, plasma, components obtained from plasma, packed red cells (PRC), transition zone material or buffy coat (BC); blood products derived from blood or a blood component or derived from bone marrow; red cells separated from plasma and resuspended in a physiological fluid or a cryoprotective fluid; and platelets separated from plasma and resuspended in a physiological

fluid or a cryoprotective fluid. The biological fluid may have been treated to remove some of the leukocytes before being processed according to the invention. As used herein, blood product or biological fluid refers to the components described above, and to similar blood products or biological fluids obtained by other means and with similar properties.

A "unit" is the quantity of biological fluid from a donor or derived from one unit of whole blood. It may also refer to the quantity drawn during a single donation. Typically, the volume of a unit varies, the amount differing from donation to donation. Multiple units of some blood components, particularly platelets and buffy coat, may be pooled or combined, typically by combining four or more units.

As used herein, the term "closed" refers to a system that allows the collection and processing (and, if desired, the manipulation, e.g., separation of portions, separation into components, filtration, storage, and preservation) of biological fluid, e.g., donor blood, blood samples, and/or blood components, without the need to compromise the integrity of the system. A closed system can be as originally made, or result from the connection of system components using what are known as "sterile docking" devices. Illustrative sterile docking devices are disclosed in U.S. Patent Nos. 4,507,119, 4,737,214, and 4,913,756.

Each of the components of the invention will now be described in more detail below, wherein like components have like reference numbers.

Figure 1 illustrated one embodiment of the filter device 100, comprising a housing 25 having an inlet 20 and an outlet 30, and defining a fluid flow path between the inlet and the outlet, wherein a filter 10, comprising a first filter element 1 and a second filter element 2, is disposed across the fluid flow path.

In accordance with the invention, the filter 10 may be configured to remove a desired amount of leukocytes. Typically, the filter is configured to remove greater than

about 90%, preferably, greater than about 99%, even more preferably, greater than about 99.9%, or more, of the leukocytes from the plasma-rich fluid passing through the filter. For example, the filter can be configured to provide a filtered fluid having about 1 x 10^4 leukocytes or less. In some embodiments, the filter can be configured to provide a filtered fluid having about 1 x 10^3 leukocytes or less.

In one embodiment, wherein the fluid to be filtered comprises platelet-poor-plasma, the resultant filtered fluid has about 200 leukocytes/liter or less, preferably, about 100 leukocytes/liter or less. In some embodiments, the filtered fluid has about 75 leukocytes/unit (e.g., a unit having a volume of about 300 ml) or less.

Preferably, the filter is configured to prevent the passage therethrough of a significant level of red blood cells, and can be configured to prevent the passage therethrough of a substantial number of platelets. In a preferred embodiment, there should be no visible indication (to the technician carrying out the filtration) of red blood cells downstream of the filter. For example, there should be no visible indication of red blood cells in the tubing leading from the outlet of the filter device to the downstream container. Typically, the filtered fluid (e.g., in the container downstream of the filter) contains less than about 5000 platelets/μL. In an illustrative embodiment, the resultant unit of filtered fluid has less than about 1 x 10^9 platelets. In one preferred embodiment, the resultant unit of filtered fluid has about 1 x 10^4 platelets, or less.

The filter is configured to filter a suitable volume of fluid in a suitable amount of time. For example, the filter can be capable of filtering about 200 to about 400 ml of fluid with a minimal effect on the overall processing time. Illustratively, in some embodiments, the filter is capable of filtering about 250 to about 350 ml of fluid in about 15 minutes, or less, e.g., in about 10 minutes.

In some other embodiments, the filter is capable of filtering about 500 to about 1000 ml of fluid in about 25

minutes, or less, preferably, about 20 minutes or less. In one embodiment, the filter is capable of filtering about 600 to about 850 ml of fluid (e.g., a unit of apheresed plasma) in about 18 minutes or less.

Preferably, the first element 1 of the filter 10, that comprises a depth filter, comprises a leukocyte depletion medium or a combined leukocyte depletion and red cell barrier medium, wherein at least some of the leukocytes are removed by adsorption. In some embodiments, the first element also removes at least some of the leukocytes by filtration.

Typically, the second element 2 of the filter 10, comprising a membrane, more preferably a microporous membrane, has a pore size that substantially prevents cells, e.g., leukocytes and/or red blood cells, from passing therethrough.

A variety of materials can be used, including synthetic polymeric materials, to produce the porous media of the first and second filter elements according to the invention, i.e., the leukocyte depletion medium, the red cell barrier medium, the combined leukocyte depletion red cell barrier medium, and the membrane. Suitable synthetic polymeric materials include, for example, polybutylene terephthalate (PBT), polyethylene, polyethylene terephthalate (PET), polypropylene, polymethylpentene, polyvinylidene fluoride, polysulfone, polyethersulfone, nylon 6, nylon 66, nylon 6T, nylon 612, nylon 11, and nylon 6 copolymers.

The first element 1, comprising at least one of a leukocyte depletion medium, a red cell barrier medium, and a combined leukocyte depletion red cell barrier medium, comprises a fibrous medium, preferably a synthetic polymeric porous fibrous medium, typically a medium prepared from melt-blown fibers, as disclosed in, for example, U.S. Patent Nos. 4,880,548; 4,925,572, 5,152,905, 5,443,743, 5,472,621, 5,582,907, and 5,670,060. The element, which can comprise a preform, can include a plurality of layers and/or media.

The first element 1 and/or the second element 2 can be treated for increased efficiency in processing a biological

fluid. For example, the first element and/or second element may be surface modified to affect the critical wetting surface tension (CWST), as described in, for example, the U.S. Patents listed above.

Preferably, the first element 1 according to embodiments of the invention, e.g., the leukocyte depletion medium, the red cell barrier medium, or the combined leukocyte depletion red cell barrier medium, has a CWST of greater than about 70 dynes/cm, more preferably, a CWST of 72 dynes or more. For example, the medium may have a CWST in the range from about 75 dynes/cm to about 115 dynes/cm, e.g., in the range of about 80 to about 100 dynes/cm. In some embodiments, the medium has a CWST of about 85 dynes/cm, or greater, e.g., in the range from about 90 to about 105 dynes/cm, or in the range from about 85 dynes/cm to about 98 dynes/cm.

Surface characteristics of the first element and/or the second element can be modified (e.g., to affect the CWST, to provide a low affinity for amide-group containing materials, to include a surface charge, e.g., a positive or negative charge, and/or to alter the polarity or hydrophilicity of the surface) by chemical reaction including, for example, wet or dry oxidation, by coating or depositing a polymer on the surface, or by a grafting reaction. Modifications include, e.g., irradiation, a polar or charged monomer, coating and/or curing the surface with a charged polymer, and carrying out chemical modification to attach functional groups on the surface. Grafting reactions may be activated by exposure to an energy source such as gas plasma, heat, a Van der Graff generator, ultraviolet light, electron beam, or to various other forms of radiation, or by surface etching or deposition using a plasma treatment. In some embodiments, the first and/or second elements can be modified as described in, for example, the U.S. patents listed above.

Typically, the first element 1 has a negative zeta potential (e.g., in the range of about -3 to about -30 millivolts, in some embodiments, in the range of about -7 to about -20 millivolts) at physiological pH (e.g., a pH of

about 7 to about 7.4).

In accordance with the invention, the first element 1 may be configured to remove a desired amount of leukocytes. Typically, the element is configured to remove greater than about 90%, preferably, in excess of about 99%, or in excess of about 99.9%, or more, of the leukocytes from the fluid passing through the filter.

One embodiment of a leukocyte depletion medium suitable for passing the plasma in about one unit of biological fluid (e.g., for passing a plasma-rich fluid such as platelet-poor-plasma) has, for example, a fiber surface area of from about 0.08 to about 1.4 M^2/g, and in some embodiments, from about 0.1 to about 0.9 M^2/g. One embodiment of an illustrative range for the relative voids volume is about 50% to about 92%, e.g., about 60% to about 89%.

In some embodiments, the first element comprises a red cell barrier medium, a red cell barrier medium and a leukocyte depletion medium, or more preferably, a combined red cell barrier leukocyte depletion medium. A red cell barrier medium, in accordance with the present invention, comprises a porous medium that allows the separation of a non-red cell-containing biological fluid, such as plasma, or a suspension of platelets and plasma, from a red cell-containing biological fluid. The red cell barrier medium prevents a significant level of the red cell-containing biological fluid from entering a container such as a satellite bag or a receiving container downstream of the barrier medium. The red cell barrier medium may allow the non-red cell-containing fluid to pass therethrough but significantly slows or effectively stops the flow of biological fluid as the red cell-containing fluid approaches the barrier medium. For example, the red cell barrier medium may allow a plasma-rich fluid to pass therethrough, abruptly stopping flow when red blood cells block the medium.

By slowing the flow of the biological fluid, the barrier medium allows the operator to manually stop the flow to

prevent the red cell-containing biological fluid from entering a container such as a satellite bag or a receiving container downstream of the barrier medium, e.g., prior to a significant level of red cells passing through the barrier medium. This embodiment of the invention allows the operator more time to intervene and stop the flow. For example, a supernatant plasma-rich fluid may flow through the red cell barrier medium at an initial rate of about 15 ml/min, but the flow may decrease to about 5 ml/min as a sediment red cell-containing fluid approaches the medium. A reduction in flow, e.g., a 33% reduction, may provide the operator sufficient time to stop the flow at the appropriate time. In some circumstances, for example, when plasma-rich fluid is expressed from a plurality of separate bags at approximately the same time, this reduction in flow allows the operator to process a greater number of containers more efficiently.

A principal function of the red cell barrier medium is to separate a red cell-containing fraction of a biological fluid from a non-red cell-containing fraction. The red cell barrier medium may act as an automatic "valve" by slowing or even stopping the flow of a red cell-containing biological fluid. In some embodiments, the automatic valve function may quickly or instantly stop the flow of the red cell-containing biological fluid, thereby obviating the need for the operator to monitor this step.

In one embodiment, a red cell barrier medium suitable for passing the plasma in about one unit of biological fluid preferably has, for example, a fiber surface area of about 0.04 to about 3.0 M^2/g, and in some embodiments, about 0.06 to about 2.0 M^2/g. One example of a suitable range for the relative voids volume is about 71% to about 93%, e.g., about 73% to about 90%.

One embodiment of a combined leukocyte depletion red cell barrier medium suitable for passing the plasma in about one unit of biological fluid preferably has a fiber surface area of from about 0.3 to about 2.0 M^2/g, e.g., from 0.25 to about 1.5 M^2/g, or from about 0.35 to about 1.4 M^2/g, e.g.,

0.4 to 1.2 M^2/g. An exemplary range for the relative voids volume is about 71% to about 93%, e.g., about 72% to about 91%, or about 75% to about 89%, e.g., 73 to 87%.

These characteristics and ranges may be adjusted or modified as necessary, e.g., for those embodiments involving different volumes of biological fluid. Illustratively, the fiber surface area and/or the voids volume utilized for the leukocyte depletion media, the red cell barrier, and the red cell barrier/leukocyte depletion media as disclosed above may be adjusted as necessary.

Exemplary leukocyte depletion media, red cell barrier media and red cell barrier/leukocyte depletion media are disclosed in, for example, U. S. Patent Nos. 4,880,548, 5,100,564, 5,152,905, 5,443,743, 5,472,621 and 5,670,060.

The second element 2 comprises at least one, and in some embodiments, no more than one, membrane. Preferably, the second element comprises a microporous polymeric membrane. Typically, the second element comprises a hydrophilic microporous polymeric membrane.

A variety of membranes are suitable for use in accordance with the invention, and a variety of polymeric materials are suitable for producing these membranes.

Illustrative suitable membranes include, but are not limited to, membranes produced from polymeric materials as described above, e.g., polyamide membranes, such as nylon membranes (including, but not limited to, nylon 6, 6T, 11, 46, 66, and 610), polysulfone membranes, such as polyarylsulfone, polysulfone, polyethersulfone, and polyarylsulfone membranes. Other suitable membranes include membranes made from, for example, polyacrylates, polyvinylidene fluoride, polypropylene, cellulose acetate, and nitrocellulose.

Suitable membranes include, for example, membranes described in U.S. Patent Nos. 4,340,479, 4,702,840, 4,707,266, 4,900,449, 4,906,374, 4,964,989, 4,964,990, 5,108,607, 5,277,812 and 5,531,893, and International Publication No. WO 98/21588.

A variety of commercially available membranes are also suitable for carrying out the invention. Suitable membranes include, but are not limited to, those available from Pall Corporation under the tradenames BIODYNE® PLUS, BIODYNE® A, BIODYNE® B, BIODYNE® C, POSIDYNE®, LOPRODYNE® LP, SUPOR®, SUPOR® 30Q, SUPOR® 30 PLUS, and PREDATOR®.

The membranes and/or polymeric materials can be unmodified or modified as described above, e.g., to affect the CWST, to provide a low affinity for amide group-containing materials and/or to include a surface charge.

Preferably, the second element has a pore structure that will substantially prevent the passage therethrough of undesirable material, e.g., large particulate matter, microaggregates and/or blood cells. For example, the second element can sieve out at least level of the undesirable material passing through the first element. Accordingly, at least one membrane typically has a pore size of about 5 micrometers or less, e.g., about 0.3 to about 4 micrometers. In one preferred embodiment, the membrane has a pore size of about 3 micrometers or less.

As noted earlier, the second element can be treated for increased efficiency in processing a biological fluid. Illustratively, in one preferred embodiment, the second element is surface modified to provide a low affinity for amide group-containing materials such as proteinaceous materials, as described in, for example, U.S. Patent Nos. 4,906,374, 5,019,260, 4,886,836, and 4,964,989. In some embodiments, the second element has an adsorption of proteinaceous material measured by the Bovine Serum Albumin (BSA) Adsorption Test of less than 100 micrograms per square centimeter. Illustratively, the second element can have an adsorption of proteinaceous material measured by the BSA Adsorption Test of less than about 50 micrograms per square centimeter, and in some embodiments, about 35 micrograms/cm^2, or less.

The second element can have any suitable thickness. For

example, in one illustrative embodiment, the second element has a thickness in the range of from about 0.002 inches to about 0.010 inches, preferably about 0.005 inches to about 0.0075 inches.

The filter 10 can include additional elements, layers, or components, that can have different structures and/or functions, e.g., at least one of prefiltration, support, drainage, spacing and cushioning. Illustratively, the filter can also include at least one additional element such as a mesh and/or a screen.

The filter, comprising the first and second elements, is typically placed in a housing 25 to form a filter assembly or filter device 100. Preferably, the filter device is sterilizable. Any housing of suitable shape to provide an inlet and an outlet may be employed. The housing may be fabricated from any suitably rigid, impervious material, including any impervious thermoplastic material, which is compatible with the fluid being processed. The housing may include an arrangement of one or more channels, grooves, conduits, passages, ribs, or the like, which may be serpentine, parallel, curved, circular, or a variety of other configurations.

Suitable exemplary housings are disclosed in U.S. Patent Nos. 5,100,564, 5,152,905, 4,923,620, 4,880,548, 4,925,572, and 5,660,731, as well as International Publication No. WO 91/04088. It is intended that the present invention not be limited by the type, shape, or construction of the housing.

Typically, the filter device or filter assembly 100 according to the invention is included in a biological fluid processing system, e.g., a system including a plurality of conduits and containers, preferably flexible containers such as blood bags. In one preferred embodiment, a system according to the invention comprises a closed system including the filter device.

Figure 2 illustrates an embodiment of a biological fluid processing system 1000, including the filter device 100, a plurality of containers 50-53, and a plurality of connectors

3, wherein the components of the system are in fluid communication with each other via a plurality of conduits. In this illustrated embodiment, the system 1000 also includes a phlebotomy needle 501 (with a cover), a phlebotomy needle protector 500, a sampling arrangement 600, a sampling arrangement needle or cannula 601 (with a cover), an additional filter device, leukocyte filter device 200, and a plurality of flow control devices 15 (such as one or more valves, clamps, or the like).

In those embodiments including a sampling arrangement 600, the arrangement is preferably arranged to minimize contamination of the collected biological fluid by allowing a first sample of the collected fluid to be passed to a location other than the collection container 50, e.g., the first sample is passed from phlebotomy needle 501 through the sampling arrangement 600 and sampling arrangement needle 601 into a sampling device (not shown) such as an evacuated stoppered container, e.g., a vacutainer.

One or more containers in the system can be suitable for holding, for example, blood components and/or additives (e.g., nutrients, storage solutions, and/or inactivation agents). The system can include additional components, such as, for example, additional filter devices, including leukocyte depletion filter devices, (with and without filter bypass loops). Additionally, or alternatively, the system can include at least one of the following: a gas collection and displacement arrangement (e.g., including a liquid barrier medium and/or a gas collection and displacement bag, as disclosed in U.S. Patent No. 5,472,621 and International Publication No. WO 93/25295), a device for processing a fluid including gas (e.g., as disclosed in U.S. Patent No. 5,451,321 and International Publication No. WO 91/17809) such as one or more gas inlets, one or more gas outlets. In some embodiments, the system includes at least one of the following: as a sampling arrangement (e.g., as disclosed in International Publication No. WO 98/28057), one or more needles and/or cannulas, and a phlebotomy needle protector.

In the embodiment of the system 1000 illustrated in Figure 2, the system includes leukocyte filter device 200, e.g., to reduce the level of leukocytes from a unit of biological fluid before further processing the fluid, or at least further processing one or more components of the fluid.

For example, in accordance with one embodiment utilizing the illustrated system, wherein flow control devices 15 are operated to allow and/or prevent flow as desired, a unit of biological fluid, e.g., a unit of whole blood, is passed from phlebotomy needle 501 into collection bag 50 and then through a leukocyte depletion filter device 200 (that may also deplete platelets from the blood) into first container or first satellite bag 51. If desired, processing the unit of whole blood can include passing gas (e.g., air) through at least one vent upstream and/or downstream of the filter device 200 and/or passing gas along a gas collection and displacement loop communicating with the inlet and outlet of the device 200.

The leukocyte-depleted (or leukocyte- and platelet-depleted) fluid in first satellite container 51, that still contains some level of leukocytes (and typically some level of platelets), is preferably centrifuged to provide a supernatant layer comprising plasma-rich fluid, and a sediment layer comprising red blood cells. Subsequently, the plasma-rich fluid (e.g., platelet-poor plasma) is passed from first satellite container 51 through the second filter device 100, i.e., the device comprising a filter 10 having first and second filter elements 1 and 2 as described above, to provide plasma-rich fluid substantially free of leukocytes and without externally visible red blood cells in second satellite container 52. In an embodiment, the filtered plasma-rich fluid is substantially free of red blood cells, leukocytes, and platelets.

The separated blood components can be further processed if desired. For example, in accordance with the embodiment of the system illustrated in Figure 2, an additive solution can be passed from third satellite bag 53 to be combined with

the red cells in second satellite bag 51, and the red cells/additive solution can be stored until needed.

EXAMPLE

As generally shown in Figure 1, a filter 10 comprising a first filter element 1 and a second filter element 2 is placed in a housing having an inlet and an outlet to provide the filter device 100, wherein the first filter element 1 is upstream of the second element 2. Each filter element is a planar circular disc having a diameter of about 47 mm.

A system is arranged as generally shown in Figure 2, e.g., the system includes a leukocyte filter device 200, the filter device 100 as described above, a collection bag 50, as well as first, second, and third satellite containers 51-53.

The first filter element comprises 8 layers of melt-blown PBT fibers, surface modified as described in U.S. Patent No. 5,152,905 using hydroxyethyl methacrylate and methacrylic acid. The first filter element has a CWST of 95 dynes/cm, and a negative zeta potential at physiological pH. The filter has no more than one membrane, as the second filter element is a single nylon 66 membrane, commercially available from Pall Corporation (East Hills, NY) under the tradename LOPRODYNE® LP, having a nominal pore size of 3 micrometers.

A unit of whole blood is collected in a collection bag 50 containing an anticoagulant, and passed through a leukocyte- and platelet-depleting filter 200 into first satellite bag 51 The filtered blood, that now has about 1 x 10^5 leukocytes in the unit, is centrifuged in the satellite bag 51 to provide a supernatant layer of platelet-poor-plasma (PPP) and a sediment layer including red blood cells. The satellite bag is placed in a plasma expressor and the PPP is expressed from the bag, through the filter device 100 (i.e., fluid is passed through the first filter element 1 and then through the second filter element 2), and into an empty second satellite bag 52. Flow stops after the "front" of red cells from the sediment layer contacts the filter, and there

are no red cells in the fluid downstream of the filter visible to the technician operating the system.

Analysis of the unit of filtered PPP shows 55 white blood cells in the total volume of PPP. There are less than about 21 platelets/μL present.

This example shows that filter devices according to the invention can provide substantially cell-free plasma.

All of the references cited herein, including publications, patents, and patent applications, are hereby incorporated in their entireties by reference.

While the invention has been described in some detail by way of illustration and example, it should be understood that the invention is susceptible to various modifications and alternative forms, and is not restricted to the specific embodiments set forth. It should be understood that these specific embodiments are not intended to limit the invention but, on the contrary, the intention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention.